REMARKS

Claims 69-70 are pending in the present application and at issue. Claim 70 has been amended to clarify the claim d invention. The scope of the claim has not changed.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 69-70 under 35 U.S.C. 112

Claims 69-70 are rejected under 35 U.S.C. 112, first paragraph, "because the specification, while being enabling for DNA encoding a Savinase or Savinase library enzyme, does not reasonably provide enablement for the broadly claimed method using a gene encoding a diversified library of protein variants." This rejection is respectfully traversed.

It is also well settled that "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971).

Moreover, "[a]ny assertion by the Patent Office that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed." *In re Dinh-Nguyen*, 181 U.S.P.Q. 46, 47 (C.C.P.A. 1974). Thus, the burden is upon the Patent Office to set forth reasonable grounds in support of its contention that a claim reads on inoperable subject matter). See *In re Stark*, 172 U.S.P.Q. 402, 406 n. 4 (C.C.P.A. 1972).

It is also well settled that a patent need not teach and preferably omits what is well known in the art. *Spectra-Physics Inc. v. Coherent Inc.*, 3 U.S.P.Q.2d 1737 (Fed. Cir. 1987).

Applicants submit that the specification complies with the enablement rejection.

The claimed invention relates to methods for selecting a variant of a protein with reduced immunogenicity. Proteins and DNA sequences encoding same are well known in the art. Furthermore, at pages 30-38, the specification describes numerous proteins for use in the methods of the present invention. Moreover, it is routine for one of ordinary skill in the art to generat libraries of variants of a pr tein, e.g., as described at pages 40-44 of the specification.

For th foreg ing r asons, Applicants submit that the claims vercome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsid ration and withdrawal of the rejection.

II. The Rejection of Claims 69-70 under 35 U.S.C. 112

Claims 69-70 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Office states:

> The specification fails to provide an adequate written description of a method for selecting a variant protein with reduced immunogenecity by screening using competitive ELISA assay. In conjunction, there is no description in the specification as to a diverse DNA library of genes that encodes a variant protein. It does not describe how a diverse DNA library of genes is generated, the source of the diverse kinds of genes and/or identification of the genes for library formation.

This rejection is respectfully traversed.

As explained in Section I above, proteins and DNA sequences encoding same are well known in the art. Furthermore, at pages 30-38, the specification describes numerous proteins for use in the methods of the present invention. Moreover, it is routine for one of ordinary skill in the art to generate libraries of variants of a protein, e.g., as described at pages 40-44 of the specification.

Moreover, competitive ELISA is a well known assay. Applicants enclose a copy of an article from Current Protocols in Immunology, which describes competitive ELISA.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 69-70 under 35 U.S.C. 112

Claims 69-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is respectfully traversed in part.

First, the Office objected to the terms "reduced," "capacity," and "diversified" as being relative terms. This rejection is respectfully traversed.

Applicants submit that these terms are clear to one of ordinary skill in the art. For example, the specification describes that a protein variant has "reduced immunogenicity" relative to the protein. Furthermore, the specification discloses that "the antibody binding capacity" is measured using competitive ELISA. Finally, the term "diversified library" would be understood by one of ordinary skill in the art as having diff rent variants.

Second, the Office objected to the term "the samples" for lacking antecedent basis. Claim 69 has been amended to provide antecedent basis for this term. Therefore, this rejection has been overcome.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. The Rejection of Claims 69-70 under the Doctrine of Obviousness-Type Double Patenting

Claims 69-70 are rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 55-73 of Application No. 09/417,608 and over claims 1-7, 11-14, 20-21 and 40 of Application No. 09/694,173. This rejection is respectfully traversed.

Claim 55 of the 608 application reads as follows:

> 55. A method of producing a protein variant, comprising the steps of:
> (a) subjecting a random peptide display package library to one or more antibodies to identify peptides that bind to the one or more of the antibodies;
> (b) identifying one or more epitope patterns by aligning the peptides that bind to the one or more of the antibodies with each other;
> (c) obtaining a three-dimensional structure of a parent protein;
> (d) identifying the one or more epitope patterns on the three-dimensional structure of the parent protein;
> (e) identifying an epitope area of amino acids situated within 5 Å of any amino acid of the one or more epitope patterns of the parent protein; and
> (f) modifying one or more amino acids identified in step (e) of the parent protein to form the protein variant, wherein the protein variant retains functionality of the parent protein and has a lower immunogenicity than the parent protein.

Claim 1 of the 173 application reads as follows:

> 1. A method for high throughput screening (HTS) of a population of host cells for production of a molecule of interest, the method comprising the steps of:
> (a) arranging the host cells in a spatial array so each position in the spatial array is occupied by one cell,
> (b) cultivating the host cells in an HTS process, wherein the host cells are cultivated under growth conditions that ensure minimal variation in the concentration or amount of the molecule of interest between all positions in the spatial array,
> (c) assaying each array position for production of the molecule of interest, and
> (d) s lecting the cells from those positions wher the molecule of inter st was produced, as determined in step c).

The claims of the 608 and 173 applications do not use competitive ELISA, as recited in the claims of the present invention. Thus, the inventions claimed herein are patentably distinct from the 608 and 173 applications.

V. The Rejection of Claims 69-70 under 35 U.S.C. 102

Claims 69-70 are rejected under 35 U.S.C. 102(b) as being anticipated by Jespers et al. (J. Mol. Biol., 269: 704-718 (1997)). This rejection is respectfully traversed.

Jespers et al. disclose a method of epitope mapping, comprising preparing a randomized library of staphylokinase mutants by error-prone PCR, phage display, and negative selection on binding to antibodies. The staphylokinase mutants were analyzed by phage ELISA.

However, Jespers et al. do not disclose a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity. Applicants therefore submit that this rejection has been overcome.

VI. The Rejection of Claims 69-70 under 35 U.S.C. 103

Claims 1-20 are rejected under 35 U.S.C. 103 as being unpatentable over Jespers et al. or Williams et al. (J. Immunological Methods, 213: 1-17 (1998)). This rejection is respectfully traversed.

Jespers et al. is discussed in Section V above.

Williams et al. disclose a method for identifying linear epitopes of beta lactoglobulin (BLG) using PEPSCAN and phage display. Specifically, Williams et al. raise an antibody against BLG and subject a library of randomized short peptides to the antibody. Williams et al. then align BLG and the nanopeptides that bind to the antibody. Williams et al. use phage ELISA to screen clones for binding to anti-BLG IgG.

However, Williams et al. also do not disclose or teach a method comprising the use of competitive ELISA to identify variants with reduced immunogenicity.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to

contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: November 19, 2003

Elias J. Lambiris, Reg. No. 33,728
Novozymes North America, Inc.
500 Fifth Avenue, Suite 1600
New York, NY 10110
(212) 840-0097